REMARKS

Reconsideration is requested.

Claims 12-33 are pending. Claim 21 has been withdrawn from consideration.

Rejoinder and allowance of claim 21 with claims 12-20 and 22-33 is requested.

A copy of the priority document will be submitted, as a courtesy to the Examiner, under separate cover. The applicants note however that a copy of the priority document has been previously submitted and a further copy should not be required, according to the MPEP.

The Section 103 rejection of claims 12-20 and 22-33 over Maertens (WO 96/04385) in view of Hofstaetter (Vax Sang, Vol. 45, pp 155-165), is traversed.

Reconsideration and withdrawal of the rejection are requested in view of the following distinguishing comments.

The applicants submit that it has been shown for the first time in the present application that removal of the cysteine shielding group allows to restore the native-like conformation of HCV envelope proteins. This was unexpected and never described before. Furthermore, the present application provides, for the first time, experimental evidence that HCV envelope proteins with reversibly blocked cysteines can be obtained (see Examples 1 and 4 of the present application). The reducing and thiol-blocking agents and the protection protocol used in the present application are not of standard use for the ordinarily skilled person in the art.

Further, neither Maertens (WO 96/04385) nor Hofstaetter provide evidence or suggest that reversible blocking of cysteines would lead to an HCV envelope protein with improved diagnostic and therapeutic properties.

Maertens, in fact, would be understood by one of ordinary skill in the art to teach away from the presently claimed invention since it describes and demonstrates irreversible blocking of the E1 and E2 protein, see page 16, lines 9-26, and Example 5. The reagent used for blocking cysteine thiol, namely NEM, causes **irreversible** blocking of cysteine thiol groups, at least the blocking group can not be removed by reducing agents such as DTT. In other words, cysteines blocked with NEM do **not** have a reversible redox status. WO96/04385 is thus not contemplating or suggesting removable cysteine thiol blocking groups such as sulphon groups. In Example 10, lines 9-11 of Maertens, it is emphasized that a good purification protocol is required to reach a high reactivity of the HCV envelope proteins with human sera. As such, the ordinarily skilled person would have been motivated to use an irreversible blocking agent in the purification process of HCV envelope proteins in order to block free thiol groups.

Hoffstaeter fails to cure the deficiencies of Maertens.

Hoffstaeter is situated in a completely different field, namely standard immunoglobulines, not HCV proteins. As such, this reference would not have suggested to the ordinarily skilled person to arrive at what is presently claimed. Moreover, Hofstaetter does not address the problem of obtaining purified HCV envelope proteins for diagnostic and therapeutic use. Further, Hofstaetter does not teach or suggest that reversible blocking of HCV envelope proteins would result in HCV envelope proteins with improved activity.

The claims are therefore submitted to be patentable over the cited combination of art and withdrawal of the Section 103 rejection is requested.

The claims are submitted to be in condition for allowance and a Notice to that effect is requested. The Examiner is requested to contact the undersigned, preferably by telephone, in the event anything further is required to place the present application in condition for allowance.

Respectfully submitted,

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